Indocyanine Green Angiography Patterns of Zones of Relative Decreased Choroidal Blood Flow in Patients With Exudative Age-Related Macular Degeneration

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■ BACKGROUND AND OBJECTIVE: To investigate the incidence and patterns of posterior zones of relative decreased choroidal blood flow in patients with exudative age-related macular degeneration.

■ PATIENTS AND METHODS: Digital indocyanine green (ICG) angiograms from 100 patients with exudative age-related macular degeneration were reviewed for the presence of posterior zones of relative decreased choroidal blood flow. The patterns of these zones and their location relative to the choroidal neovascular process were noted.

■ RESULTS: Ninety-five percent of the angiograms displayed the presence of either a complete or an incomplete zone of relative choroidal hypoperfusion.

INTRODUCTION

The choroidal vascular bed has been described as a rich anastomotic network of choroidal arteries and veins.1-3 Hayreh has studied fluorescein angiograms in monkeys and humans, and has suggested that the choroidal vascular system is segmental and end-arterial.3-5 Using indocyanine green (ICG) angiography, this study investigated the choroidal vascular pattern of flow in patients with choroidal neovascular disease in the setting of age-related macular degeneration.

ICG is a tricarbocyanine dye with its peak absorption (805 nm) and peak fluorescence (835 nm) in the near-infrared spectrum.6,7 It is more highly protein bound (98%) than sodium fluorescein (60% to 80%). Hence, sodium fluorescein will leak from the fenestrated choroidal vessels, and ICG dye will remain intravascular. These properties of ICG dye allow superior images of choroidal blood flow.7,9

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PATIENTS AND METHODS

Digital ICG angiograms obtained from 100 consecutive patients with exudative age-related macular degeneration were reviewed for the presence of areas of relative decreased choroidal blood flow and the relative location of these areas to the choroidal neovascularization. All of the angiograms were reviewed by two independent observers (MFG and RSD).

The ICG dye was reconstituted to a concentration of 25 mg/cc, of which 2 cc was injected intravenously and then followed by a 5-cc saline flush. Images were obtained with a Candella ICG videoangiography system using a diode laser illumination source. Care was taken to obtain early transit choroidal images beginning approximately 10 seconds after dye injection. The patients had routine fluorescein angiograms performed immediately prior to the ICG angiograms.

RESULTS

A zone of relative decreased choroidal blood flow was identified in 95% of all cases studied. These zones were most apparent in the earliest images obtained,
within an average of 10 to 20 seconds. In 5% of these cases a choroidal zone of hypoperfusion was not identified due to the poor quality of images obtained.

Five patterns of relative decreased choroidal blood flow were identified, as illustrated in Figures 1 through 13: horizontal (32%), vertical (14%), bipartite (9%), tripartite (31%), and quadripartite (9%). These patterns were further classified as complete or incomplete. Areas of apparent choroidal neovascularization were localized within or at the edges of the zones of relative choroidal hypoperfusion in all patients in whom such zones were identified. No association between the area of reduced choroidal perfusion and the size of choroidal neovascularization was found.

**DISCUSSION**

The choroidal vascular network has been described from latex cast studies as consisting of a freely anastomotic system of arterioles and venules. Using fluorescein angiographic studies of monkeys and humans, Hayreh proposed a segmental pattern of
blood flow within the choroid within which the posterior ciliary arteries behave essentially as end-arteries. As with other end-arteries in the body, this implies the presence of watershed areas of relative hypoperfusion. He further postulated that the macular region was a watershed zone of vascular convergence to explain the localization of choroidal neovascularization within the macula of patients with age-related macular degeneration.

The advent of ICG angiography has allowed us to study the choroidal vasculature in vivo. ICG techniques employ near-infrared wavelengths that allow visualization of the choroidal fluorescence and eliminate blockage due to overlying pigment or hemorrhage. Takahashi et al. demonstrated with ICG angiography that a peripheral watershed zone is a regular feature in the temporal retinal periphery. These areas of decreased choroidal blood flow were felt to represent the terminal branches of peripheral retrograde ciliary arteries anteriorly and short posterior ciliary arteries posteriorly. Hayashi and de Laey were able to demonstrate watershed zones of choroidal vascular flow or regions of local hypofluorescence on ICG angiography in 10 of 27 eyes studied. They postulated these areas of reduced choroidal filling to be secondary to either insufficient choroidal blood flow or a reduc-
tion in the numbers of choroidal vessels. In either case, they believed an area of choroidal insufficiency was present that may then induce the choroidal neovascular response.\textsuperscript{13,14}

Yannuzzi et al. reported the presence of watershed zones of choroidal blood flow in 12 of 129 patients studied using ICG.\textsuperscript{15} In those patients with demonstrable watershed zones, they localized the choroidal neovascular process on the perfused side of the edges of these zones. One patient received laser treatment directed in a scatter fashion to the area of relative nonfilling choroid with subsequent regression of the subfoveal choroidal neovascular membrane.

The exact nature of these apparent zones of relative choroidal hypoperfusion is not clear at this time. Although they may be in part related to an anatomic compartmentalization of the choroidal vascular tree, they may also represent normal physiologic gradients of relative hypoperfusion. The incidence of such zones in young patients and in patients without age-related macular degeneration is not known. Ross et al. recently reported an increased incidence of areas of presumed choroidal hypoperfusion in patients with age-related macular degeneration and suggested a causal association.\textsuperscript{16} It is possible that we found a higher percentage of areas of relative choroidal nonfilling than prior studies due to the care we took to obtain very early transit ICG images. This has allowed us to recognize multiple patterns of decreased choroidal blood flow.

The localization of choroidal neovascularization to these areas of apparent decreased choroidal blood flow is striking. Possible roles of these zones of relative choroidal hypoperfusion in the pathophysiology of the development of choroidal neovascularization would be conjectural at this time. Potential therapeutic implications of this phenomenon are also currently unproven. Nevertheless, further studies of choroidal hypoperfu-
sion using this technique have the potential to add significantly to our understanding of the pathophysiology of choroidal neovascularization and its management.

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REFERENCES